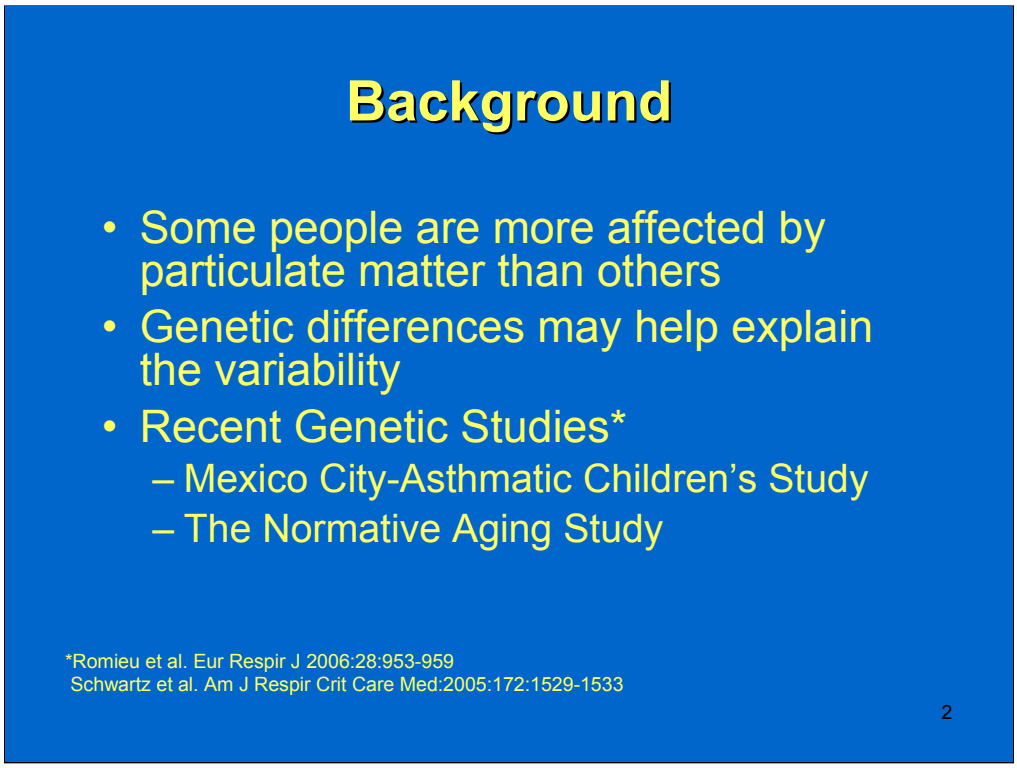
Effects on the Heart from PM Exposure and a Possible Role of Genetics

April 24, 2008

California Air Resources Board

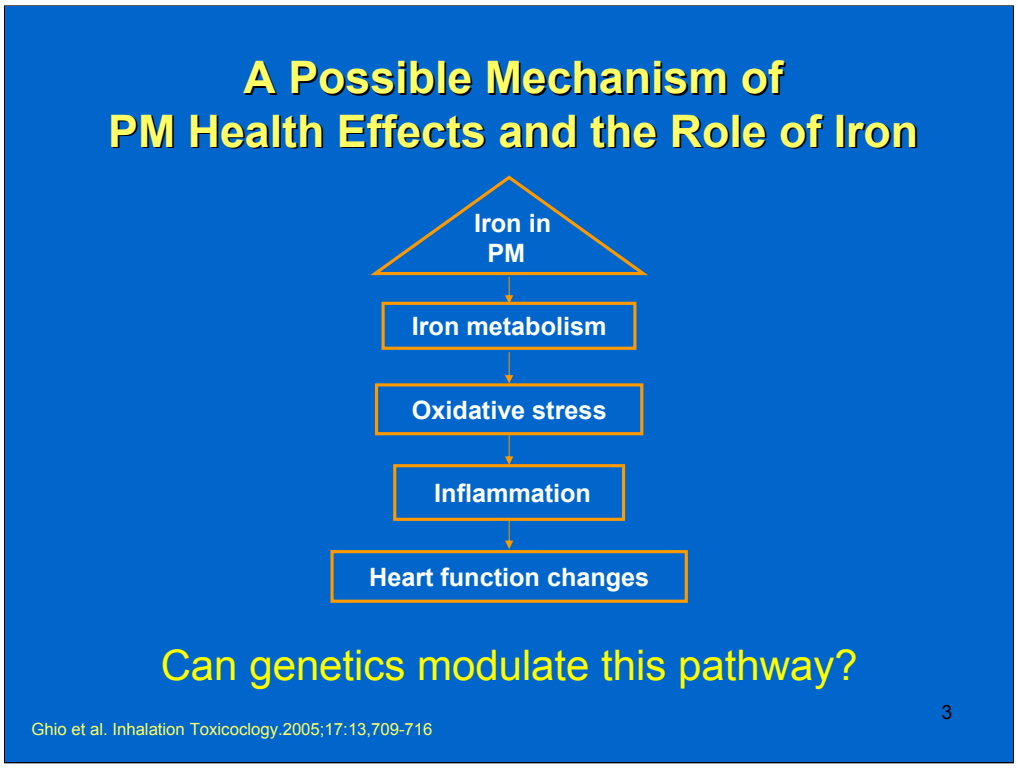
California Environmental Protection Agency

Thank you Mr. Goldstene and good morning Chairman Nichols and members of the Board. In today's health update we will be presenting a paper that examines changes in heart function with exposure to fine particulate matter. Specifically, the investigators studied how genes involved in iron metabolism may affect the toxicity of fine PM.



Exposure to particulate matter has been associated with a number of adverse health effects including hospitalizations and premature death. However, there is considerable evidence that some people are affected by particulate air pollution more than others, although little is known about the basis of this variability. Factors such as asthma, diabetes and heart disease, as well as age, occupation and access to health care may contribute to this difference among individuals.

One important area of research is to determine if genetic differences make individuals more vulnerable to air pollution impacts. A recent study from Mexico City indicated that asthmatic children with a certain gene mutation appear to be more susceptible to developing respiratory symptoms related to ozone exposure. The same gene mutation was studied in the Normative Aging Study, which is the original study group of today's highlighted publication. That study found an association between exposure to PM and reduced heart function in elderly men that was related to the genetic make-up of the individuals.



How PM causes these serious adverse health effects is an active area of research. Numerous studies have provided evidence for many different possible pathways by which particles can affect human health.

This slide describes only one of these possible mechanisms and includes a role for iron, which is abundant in fine particles, PM2.5. It is proposed that when iron reacts with oxygen in the body, it can cause oxidative stress, which damages cells of the lungs. This in turn leads to inflammation and eventually causes changes in the way the heart functions. The study for this health update examined the role of genes in this disease pathway.

Methods

- 518 men from the Normative Aging Study
- Tested for two forms of HFE gene
  - Involved in iron metabolism
  - Common form (336 men)
  - Variant form (182 men)
- Air pollutants measured
  - Fine particulate matter (PM2.5)
  - Black carbon, sulfate, ozone
- Health outcome
  - Heart rate variability (ability of the heart to respond to environmental stresses)
  - Decreased heart rate variability can be a risk factor for heart disease

Park et al. HFE Genotype, Particulate Air Pollution, and Heart Rate Variability: A Gene-Environment Interaction. Circulation.2006;114:2798-2805. Funded by National Institute of Environment Health Sciences and US EPA

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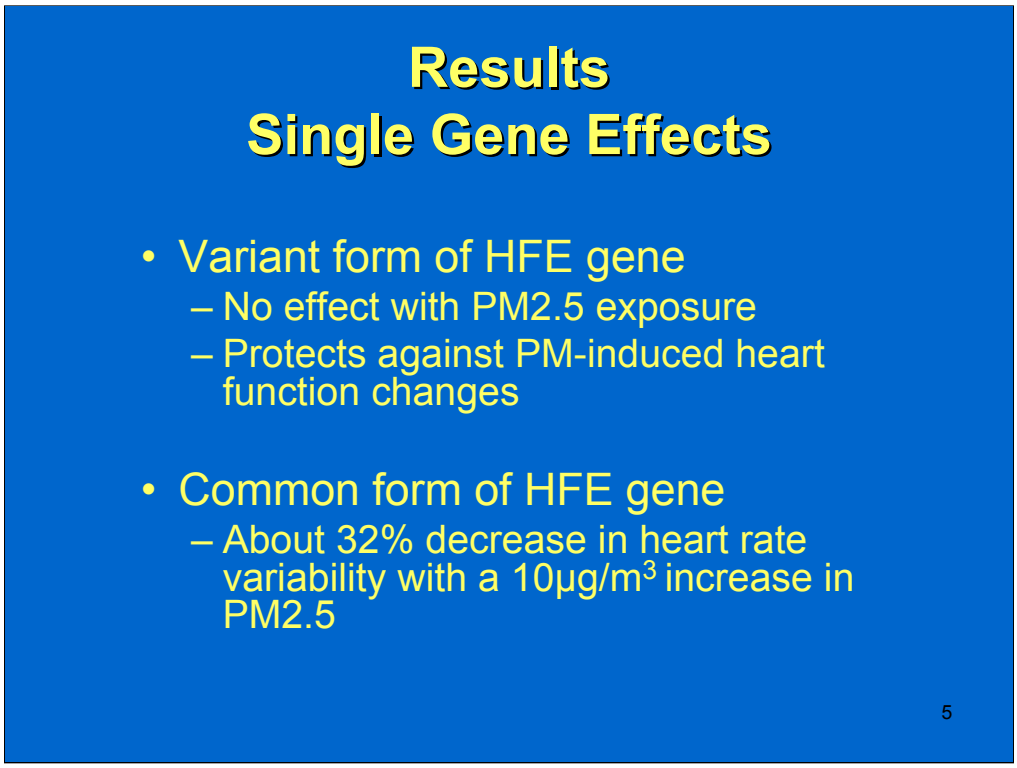
The study we are presenting today involved 518 older men, with an average age of 73 years from the Normative Aging Study in the Boston area. These men were tested for the variant and the common form of an iron metabolism gene, HFE, and were followed from the year 2000 to 2004. Ambient PM2.5, black carbon, sulfate and ozone were measured.

Heart rate variability was the only health outcome assessed and is defined as a measure of the variations in the beat-to-beat intervals of heart rate. The heart needs to be able to respond to stresses on the cardiovascular system. So heart rate variability can be an important indicator reflecting the individual's capacity to adapt effectively to environmental demands.

Decreased heart rate variability is the inability of the heart to respond to stresses. Typically reductions in heart rate variability have been reported to be linked to cardiovascular disease.

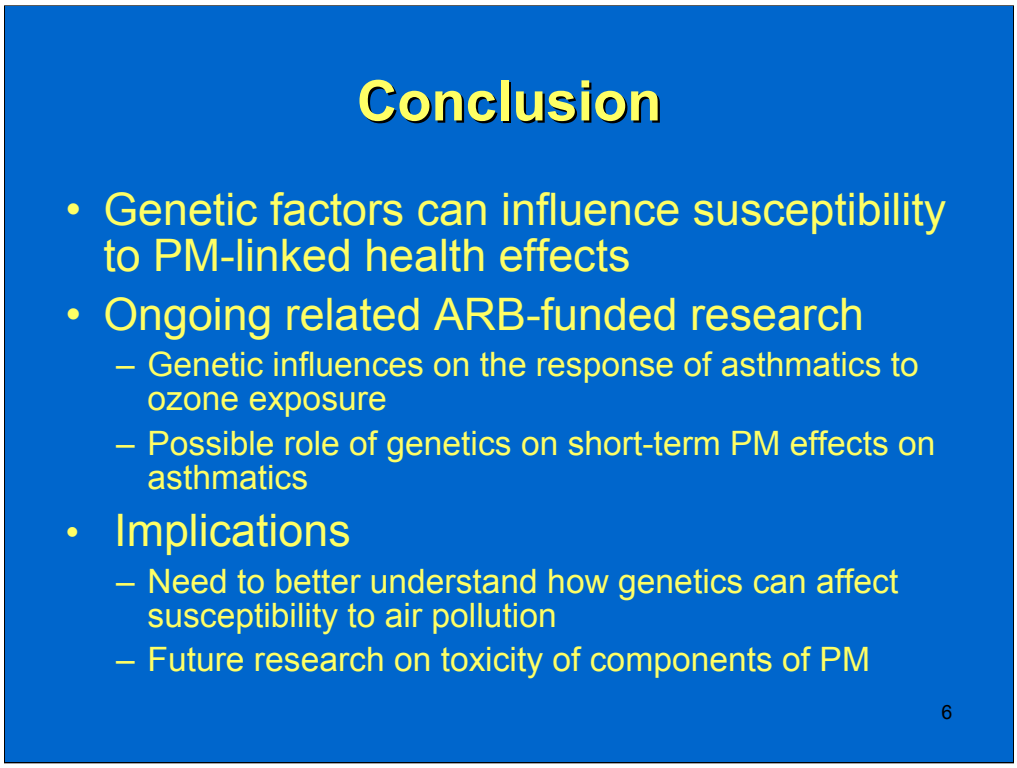
Note: Zareba et al. Cardiovascular Effects of Air Pollution: What to Measure in ECG? Environ Health Perspect.109:533-538.2001.



The study found that men with this variant form of the HFE gene showed no change in the heart rate variability when exposed to PM2.5. The investigators speculate that individuals having the variant form store more iron in the body and may tend to take up less iron from fine PM, and so were protected from PM induced heart function changes.

On the other hand, men with the common form of the HFE gene have normal iron stores in their body and had about a 32% decrease in heart rate variability with a 10μg/m^3 increase in PM2.5. The authors indicated that this was a statistically significant effect.

Note: However, in this study, the investigators did not measure iron levels in the body or the concentration of iron in fine PM.



These results provide additional evidence for the role of genetics in modulating the response to PM exposure and suggest that some populations are more sensitive to PM exposure than others.

One goal of the ARB is to investigate the impact of air pollution on sensitive populations. The Board is currently funding two research projects focused on the role of genetics on individual responses to air pollution. One of these studies is a controlled human exposure study investigating the influence of genetic mutations on ozone-induced responses in adult asthmatics. Another controlled human exposure study will investigate the role of genetics in short-term respiratory effects of PM exposure on asthmatics.

The results from the current study and from previous studies suggest that we need to consider multiple factors including the genetic make-up of individuals when we assess how people respond when exposed to PM.

Also, the results suggest that the presence of iron in PM may increase its toxicity in some populations, and point to the need for additional research to determine the relative toxicity of the various components of PM.

Thank you for your attention. We would be pleased to answer any questions you may have.